Chapter 3: Hepatitis A

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I. Disease description

Hepatitis A is caused by infection with the hepatitis A virus (HAV), a non-enveloped RNA agent that is classified as a picornavirus.[1] HAV replicates in the liver, is shed in the feces, and peak titers occur during the 2 weeks before and 1 week after onset of illness. Virus is also present in serum during this period, although in concentrations several orders of magnitude less than in feces. Therefore, the most common mode of HAV transmission is fecal-oral with the virus being transmitted from person-to-person between household contacts or sex partners, or by contaminated food or water. Because virus is present in serum during acute infection, blood-borne HAV transmission can occur, but it has been reported infrequently.

The incubation period of hepatitis A is 15–50 days, with an average of 28 days. The illness caused by HAV infection typically has an abrupt onset of signs and symptoms that include fever, malaise, anorexia, nausea, abdominal discomfort, dark urine and jaundice. Hepatitis A usually does not last longer than 2 months, although some persons may have prolonged or relapsing signs and symptoms for up to 6 months. The likelihood of having symptoms with HAV infection is directly related to age. Among children <6 years of age, most infections are asymptomatic; among older children and adults, infection is usually symptomatic. HAV infection occasionally produces fulminant hepatitis A. The case-fatality rate among reported cases of all ages is approximately 0.3%, but can be higher among older persons (approximately 2% among persons >40 years of age).

HAV infection does not result in chronic infection or chronic liver disease.

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II. Background

In the United States, hepatitis A has occurred in large nationwide epidemics approximately every 10 years, with the last increase in cases in 1995.[2] In the United States in 1997 approximately 30,000 persons were reported to have hepatitis A. Among cases reported to CDC, the most frequently reported risk factor is household or sexual contact with a person with hepatitis A (12%-26%). Approximately 11%-16% of reported cases occur among children or employees of day care centers or their contacts. However, this may represent an overestimate of the proportion of persons who acquired their infections in this setting; hepatitis A cases are ascribed to day care center-related contact without requiring that the contact have hepatitis A or that a case of hepatitis A be identified in the day care center. Additional risk factors include recent international travel (5%) and association with a suspected food or waterborne outbreak (5%). Many persons with hepatitis A do not identify risk factors (45%); their source of infection may be other infected persons who are asymptomatic of have unrecognized infection. Based on testing from the Third National Health

and Nutrition Examination Survey (NHANES III) survey conducted in 1988-1994, the prevalence of total antibody to HAV (anti-HAV) among the general U.S. population is 33%.

Most hepatitis A cases in the United States occur in the context of community wide epidemics. Communities which experience such epidemics can be classified as having high or intermediate rates of hepatitis A .

Communities with high hepatitis A rates typically have epidemics every 5–10 years that may last for several years, with substantial rates of disease (as high as 2,000 cases per 100,000 population annually during outbreaks), and few cases among persons >15 years of age. These communities often are relatively well-defined either geographically or ethnically and include American Indian, Alaskan Native, and selected Hispanic, migrant and religious communities.

In communities with intermediate rates, hepatitis A cases occur primarily among children, adolescents, and young adults. Epidemics often occur at regular intervals and persist for several years with rates typically between 50–200 cases per 100,000 per year. However, some communities experience sustained elevated rates. Often cases are concentrated in specific census tracts or neighborhoods within a larger community.

These communities with high and intermediate hepatitis A rates are concentrated in a limited number of states primarily located in the western and southwestern parts of the United States. In these areas, hepatitis A rates are consistently elevated, and cases reported from these areas account for the majority of reported hepatitis A cases nationwide. For example, during 1987-97, 50% of reported hepatitis A cases were from states with average annual disease rates at least twice the national average, yet the total population of these states represented approximately 22% of the U.S. population.

Hepatitis surveillance is essential so that disease prevention activities can be appropriately implemented and evaluated.

Hepatitis surveillance systems, with collection of demographic and risk factor data on cases, are essential for identifying areas with consistently elevated hepatitis A rates, so that disease prevention activities may be appropriately implemented and their effectiveness evaluated.

III. Importance of rapid identification

Rapid identification and prompt reporting of cases of hepatitis A are important because preventive measures can be taken to prevent transmission to other persons.

Post-exposure prophylaxis

Standard immune globulin (IG, formerly called gamma globulin) is a solution of antibodies prepared from human plasma. It is made with a serial ethanol precipitation procedure which has been shown to inactivate hepatitis B virus (HBV) and human immunodeficiency virus. When administered intramuscularly before exposure to HAV, or within 2 weeks after exposure, IG is >85% effective in preventing hepatitis A.

IG should be given to exposed persons as soon as possible, but not more than 2 weeks after the exposure. Recipients may include 1) persons with close contact (household or sexual) to a person with hepatitis A; 2) staff and attendees at child care centers where a hepatitis A case is recognized; and 3) selected common-source exposure situations (e.g., to patrons at a food establishment with an HAV-infected food handler, if the risk of transmission is determined to be high).[3]

IV. Importance of surveillance

Disease surveillance should be used to 1) identify contacts of cases who require post-exposure prophylaxis; 2) detect outbreaks; 3) determine the effectiveness of hepatitis A vaccination; 4) monitor disease incidence in all age groups; 5) determine the epidemiologic characteristics of infected persons, including the source of their infection; and 6) assess and reduce missed opportunities for vaccination. Surveillance for hepatitis A depends upon an understanding of the local epidemiology of hepatitis A.

V. Disease reduction goals

The proposed disease reduction goal for hepatitis A calls for reducing the incidence of reported cases from a baseline of 11.3 cases per 100,000 reported in 1997 to no more than 5 cases per 100,000 by the year 2010.

VI. Case definition

Clinical case definition:

An acute illness with a discrete onset of symptoms, and jaundice or elevated serum aminotransferase levels.

Laboratory criteria:

IgM anti-HAV positive.

The following case definition for hepatitis A has been approved by the Council of State and Territorial Epidemiologists (CSTE), and was published in May 1997 (Appendix 1).[4]

Clinical case definition

An acute illness with

- A discrete onset of symptoms, and
- Jaundice or elevated serum aminotransferase levels

Laboratory criteria for diagnosis

- Immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) positive

Case classification

Confirmed. A case that meets the clinical case definition and is laboratory confirmed or a case that meets the clinical case definition and occurs in a person who has an epidemiologic link with a person who has laboratory-confirmed hepatitis A (i.e., household or sexual contact with an infected person during the 15-50 days before the onset of symptoms).

VII. Laboratory Testing

Serologic Testing

IgM anti-HAV. Virtually all patients with acute hepatitis A have detectable IgM anti-HAV. The diagnosis of acute HAV infection is, therefore, confirmed during the acute or early convalescent phase of infection by the presence of IgM anti-HAV in serum. IgM anti-HAV generally disappears within 6 months after onset of symptoms.

Total anti-HAV. IgG anti-HAV appears in the convalescent phase of infection, remains for the lifetime of the person, and confers enduring protection against disease. The antibody test for total anti-HAV measures both IgG anti-HAV and IgM anti-HAV. Persons who are total anti-HAV positive and IgM anti-HAV negative have serologic markers indicating immunity consistent with either past infection or vaccination. Commercial diagnostic tests are widely available for the detection of IgM and total (IgM and IgG) anti-HAV in serum.

CDC Laboratory special studies

Occasionally, molecular virology methods such as polymerase chain reaction (PCR)-based assays are used to amplify and sequence viral genomes. These assays may be helpful to investigate common source outbreaks of hepatitis A. Providers with questions about molecular virology methods should consult with their state health department or the Hepatitis Branch, CDC. For additional information on laboratory-support for surveillance of vaccine-preventable diseases, see Chapter 19.

Serologic testing is necessary to establish a diagnosis for a person with symptoms of acute hepatitis.

VIII. Reporting

In the United States, case reports of viral hepatitis are classified as hepatitis A, hepatitis B, or hepatitis C/non-A, non-B hepatitis. Serologic testing is necessary to determine the etiology of viral hepatitis and case reports should be based on laboratory confirmation (see above). Each state and territory has regulations and/or laws governing the reporting of diseases and conditions of public health importance (Appendix 2).[5]

These regulations/laws list the diseases and conditions which are to be reported and describe those persons or groups who are responsible for reporting such as health-care providers, hospitals, laboratories, schools, day care facilities, and other institutions. Contact your state health department for reporting requirements in your state.

Reporting to CDC

There are two national reporting systems for acute viral hepatitis, the National Notifiable Diseases Surveillance System (NNDSS) and the Viral Hepatitis Surveillance Program (VHSP).

National Notifiable Diseases Surveillance System. Case reports of acute hepatitis A and other diseases are transmitted by the state health department weekly to CDC via the National Electronic Telecommunications System for Surveillance (NETSS) and include basic demographic information (excluding personal identifiers) — age, race/ethnicity, sex, date of onset, date of report, county of residence. It is important to ensure that all acute case reports have a discrete date of onset of illness, clinical evidence of hepatitis (jaundice or elevated serum aminotransferase levels), and appropriate serologic test results before transmission to CDC by the state health department.

Viral Hepatitis Surveillance Program. The VHSP, in addition to collecting basic demographic information, also collects serologic and risk factor data on cases. The case investigation worksheet (Appendix 7) and form (Appendix 8) should be filled out for all NNDSS case-reports of acute hepatitis A. VHSP forms can be obtained from the state health department or the Hepatitis Branch, CDC, 404-639-2339. VHSP case investigations should be conducted within 2 weeks from the date of onset of illness so appropriate prophylaxis can be given to household and sexual contacts. VHSP forms should be sent to the Hepatitis Branch, CDC, by the state health department within 1 month of the date of the report, or as indicated in your state. In many states, VHSP data can be entered on supplemental screens in NETSS and transmitted electronically to CDC.

Information to collect

The following information is epidemiologically important to collect in a case investigation. Additional information may also be collected at the direction of the state health department.

- Demographic information
- Clinical details including
  - —Date onset of illness
  - —Symptoms including pain, jaundice
- Laboratory results
- Vaccination status
- Risk factors
- Contact investigation and prophylaxis

IX. Vaccination schedules

Immune globulin (for hepatitis A post-exposure prophylaxis)

For persons with recent exposure (within 2 weeks) to HAV who have not previously received hepatitis A vaccine, a single intramuscular dose of IG (0.02 mL/kg) should be given as soon as possible, but not more than 2 weeks after the exposure. Pregnant women and infants should receive IG that does not

contain thimerosal. Persons who have received one dose of hepatitis A vaccine at least 1 month before a HAV exposure do not need IG.

Hepatitis A vaccine

Two inactivated hepatitis A vaccines are commercially available: HAVRIX® (SmithKline Beecham Biologicals) and VAQTA® (Merck and Co.). Both vaccines are licensed for persons ≥2 years of age. The vaccines should be administered by intramuscular injection in the deltoid muscle, with a needle length appropriate for the person's age and size.

The dose of HAVRIX® is quantified in ELISA units (EL.U.). HAVRIX® is currently licensed in a two-dose schedule of 720 EL.U. per dose (0.5 mL) for children and adolescents (2–18 years of age) and 1440 EL.U. per dose (1.0 EL.U.) for adults (>18 years of age) (Table 1).

The dose of VAQTA® is quantified in units (U). The dose and schedule for children and adolescents (2–17 years of age) is 25 U per dose in a two-dose schedule, and for adults (>17 years of age), 50 U per dose in a two-dose schedule (Table 2).

X. Enhancing surveillance

A number of activities can improve the detection and reporting of hepatitis A cases and improve the comprehensiveness and quality of reporting. Chapter 16 describes some general activities for enhancing surveillance and some specific recommendations for hepatitis A are listed below.

Appropriate serologic testing. Surveillance for acute hepatitis is challenging for several reasons. There are five different viruses (A-E) that account for nearly all human viral hepatitis. Because the clinical features of acute hepatitis caused by these viruses are similar, serologic testing is necessary to establish a diagnosis for a person with symptoms of acute hepatitis. Secondly, acute infection with several of the hepatitis viruses (HBV, HCV, and HDV) progresses to chronic infection, and review of serologic and clinical information of patients is necessary to make the differentiation between acute and chronic disease. A lack of understanding about the epidemiology of these diseases and underutilization of serologic testing may result in significant misclassification in reporting of acute viral hepatitis. For example, a provider may diagnose a child with jaundice as having hepatitis A and not order serologic testing, when in fact the child may have another illness.

To ensure accurate reporting of viral hepatitis and appropriate prophylaxis of household and sexual contacts, all case reports of viral hepatitis submitted to NNDSS should be investigated to obtain serologic testing information and risk factor data, and should be reported by the state health department to the CDC through VHSP.

Aggressive case-investigations of persons with acute disease provides the best opportunity to administer post-exposure prophylaxis to contacts.

Provider education. Providers should be educated about the importance of reporting all cases of acute hepatitis. A common risk factor for persons with acute infection is contact with a previously identified case.

Case investigation. Identifying risk factors among persons with acute disease can help better define the epidemiology of viral hepatitis at the state and local level. For example, recognition of hepatitis A outbreaks in day care centers, among homosexual men, or among injecting drug users can help target hepatitis A vaccination efforts. Analysis of VHSP risk factor data can identify populations where targeted interventions may be needed.

Laboratory reporting. Laboratories should be encouraged to report all persons with acute hepatitis. All IgM anti-HAV positive results should be reported. To facilitate reporting, these IgM results could be included in the state's list of conditions reportable by laboratories.

Hospital-based reporting. Hospitals and infection control practitioners should be encouraged to report all persons with the ICD diagnosis codes of 151 *.*, acute hepatitis. These patients may then be investigated to determine if they are indeed cases.

XI. Case investigation

Guidelines for investigating a suspected case of viral hepatitis include 1) determining a discrete onset of illness; 2) confirming evidence of acute liver disease (jaundice or elevated aminotransferase levels); and 3) obtaining serologic laboratory results. A VHSP case investigation form (Appendix 8), requesting information about demographics, laboratory data, and risk factors should be completed and sent to CDC by the state health department. On the reverse side of the VHSP form there is a viral hepatitis worksheet (Appendix 7), which may be used as a guide to assist in the case investigation.

For hepatitis post-exposure prophylaxis of contacts, see Section III. ❖

Table 1. Recommended doses of HAVRIX® (hepatitis A vaccine, inactivated)*

Group	Age	Dose (EL.U.)[¶]	Volume	No. doses	Schedule[§]
Children and adolescents	2–18 years	720	0.5 mL	2	0, 6–12
Adults	>18 years	1,440	1.0 mL	2	0, 6–12

* SmithKline Beecham Pharmaceuticals
[¶] Enzyme-linked immunosorbent assay units
[§] Months; 0 months represents timing of the initial dose; subsequent number(s) represent months after the initial dose.

Table 2. Recommended doses of VAQTA® (hepatitis A vaccine, inactivated)[£]

Group	Age	Dose (U)[¶¶]	Volume	No. doses	Schedule[§§]
Children and adolescents	2–17 years	25	0.5 mL	2	0, 6–18
Adults	>17 years	50	1.0 mL	2	0, 6

[£] Merck & Co., Inc.
[¶¶] Units
[§§] Months; 0 months represents timing of the initial dose; subsequent number(s) represent months after the initial dose.

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